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EXAMINER	
EPPERSON, JON D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 01/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/052,942	ZAUDERER ET AL.	
	Examiner	Art Unit	
	Jon D Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-84* is/are pending in the application.

4a) Of the above claim(s) *21,23,28,36,37,39,42,43,45-58 and 63-84* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20,22,24-27,29-35,38,40,41,44 and 59-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/6/04; 11/6/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. Receipt is acknowledged of a Response to a Restriction Requirement, which was dated on November 8; 2004.

Status of the Claims

2. Claims 1-84 were pending in the present application. Applicants amended claims 66 and 82. No claims were added or canceled. Therefore, claims 1-84 are currently pending.

3. Applicant's response to the Restriction and/or Election of Species requirements in the 11/8/04 Response is acknowledged (Applicant elected ***with traverse*** Group I, claims 1-45, 48-65 and 69-80) and claims 46-47, 66-68 and 81-84 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

4. Please note: Applicant's elected species (Subgroup 1 = HeLa cell; Subgroup 2 = human source; Subgroup 3 = soluble IgG, which is not a single chain; Subgroup 4 = linear double stranded vaccinia virus which is not attenuated and is not deficient in D4R synthesis; Subgroup 5 = constitutive T7 phage promoter, which is not early/late promoter and is not associated with a suicide gene; Subgroup 6 = T7 phage promoter that is under control of T7 polymerase, which is

not a transcriptional termination region; Subgroup 7 = suicide death phenotype) were found in the art, see rejections below. Applicants' elected species (Subgroup 8 = SV40 large T antigen nuclear localization signal) were not found in the art. Applicant is reminded of MPEP § 803.02 with respect to species elections:

> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, ***will not be extended unnecessarily to cover all nonelected species.*** Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

5. Claims 21, 23, 28, 36, 37, 39, 42, 43, 45, 48-52, 53-58, 63-65, 69-80 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species, the requirement having been traversed in Paper No. 6 (see below i.e., ***Response to Restriction and/or Election of Species***). Please note that claims 48 and 52 are also withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species because Applicants' elected modified phenotype is not "nonadherence" as indicated in claim 48, but rather "cell death caused by expression of suicide gene" (e.g., see 11/8/04 Response, page 5, subgroup 7). In addition, Applicants' elected species for modified phenotype is not a "combination" of "nonadherence" and "cell death" as disclosed in claim 52. Thus, the examiner does not agree that claims 48 and 52 read on the elected species (e.g., see 11/8/04 Response, page 5, subgroup 7).

6. Therefore, claims 1-20, 22, 24-27, 29-35, 38, 40-41, 44 and 59-62 are examined on the merits in this action.

Response to Restriction and/or Election of Species

7. Applicant's election of Group I (i.e., claims 1-45, 48-65 and 69-80) ***with traverse*** is acknowledged.

8. The traversal is on the ground(s) that **[1]** Groups I-V represent "related" subject matter (e.g., see 11/8/04 Response, paragraph bridging pages 1-2) and **[2]** *assuming arguendo* that Groups I-V represent distinct or independent invention, there would be no search burden on the Examiner and cite MPEP § 803 in support of this argument (e.g., see 11/8/04 Response, pages 2-3).

9. These arguments were fully considered but were not found persuasive. **[1]** First, the Examiner notes that the mere presence of any alleged overlapping subject matter would not constitute a coextensive search because each Group would have to be searched to its full extent and not just to the extent of any overlapping subject matter, which would, as a practical matter, encompass non-overlapping subject matter and hence result in a non-coextensive search. **[2]** In addition, as stated in the Restriction Requirement dated October 7, 2004 (e.g., see paragraphs 3-10), these inventions (Groups I-V) have acquired a separate status in the art as shown by their different classification and/or divergent subject matter. The different methods and/or products would require completely different searches in both the patent and non-patent databases, and

there is no expectation that the searches would be coextensive. Therefore, this does create an undue search burden for the Office.

10. Applicant's election of species in the 11/8/04 Response ***with traverse*** is also acknowledged.

11. The election of species traversal is on the ground(s) that **[1]** there is no burden in searching the rest of the species either and cite MPEP § 806.04, § 806.05 and § 803 in support of this position (e.g., see page 28, especially the last paragraph wherein Applicants state, for example, that a "search of IgG as an immunoglobulin would provide useful information regarding other types of immunoglobulins, such as IgM" i.e., there is overlapping subject matter) and **[2]** further Applicants assert the right to have additional species examined in the event that a generic claim is found to be allowable in accordance with 37 C.F.R. § 1.141(a)" (e.g., see 11/8/04 Response, page 6).

12. These arguments were fully considered but were not found persuasive. **[1]** The Examiner's position is that the species are distinct, each from the other, because the structures and modes of action of each of the species encompassed are different. They would also differ in their reactivity and/or mechanism and/or the products made. Therefore, the species have different issues regarding patentability and represent patentably distinct subject matter. Furthermore, the Examiner previously stated that should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence

now of record showing the species to be ***obvious variants*** or ***clearly admit*** on the record that this is the case. This has not been done. **[2]** In addition, it was also stated that upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

13. As a result, the restriction requirement and/or election of species is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

14. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98 (b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on the form PTO-892, they have not been considered.

15. The references listed on applicant's PTO-1449 form have been considered by the Examiner. A copy of the forms are attached to this Office Action (e.g., IDS filed 8/6/04 and 11/6/02). **Please note:** the 9/22/03, 7/1/03 and 8/13/02 IDS sheets have not been signed because these submissions are of poor quality and cannot be read. The Examiner respectfully requests new copies for these submissions.

Specification

16. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claims Rejections - 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 1-20, 22, 24-27, 29-35, 38, 40-41, 44 and 59-62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 USC 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a written description rejection.

Applicants' claims encompass a broad genus. For example, the claimed invention outlines method steps for selecting polynucleotides, which encode an intracellular immunoglobulin molecule, or fragment thereof. The scope of this claim includes an enormous number of methods using an enormous number of potential vectors wherein

said vectirs are not limited in any way (e.g., see specification, page 54, paragraph 223, "In constructing antibody libraries in eukaryotic cells, any standard vector which allows expression in eukaryotic cells may be used"; see also paragraph 124 reciting a large "laundry list" of potential examples e.g., plant, animal, RNA, DNA, etc.) produced by an unspecified number of methods (e.g., homologous recombination, direct ligation, etc.). Consequently, the nature of the invention cannot be fully determined. Although the specification discloses examples of "tri-molecular combination" using "two" non-overlapping fragments of the cleaved v7.5/tk or vEL/tk using only "vaccinia virus" genomes produced using NotI/ApaI restriction enzymes and "one" transfer plasmid containing TKL/TKR and immunoglobulin genes encoding both heavy and light chains (e.g., see page 9, paragraphs 23-24; see also Summary of Invention, paragraph 27; see also page 151, paragraph 363), the specification and claims do not provide ***any*** examples for other processes like direct ligation and homologous recombination that would likewise yield a "library" of antibodies upon expression. Therefore, the Examiner contends that Applicants have not provided a "representative" number of examples to show that they were in possession of the full scope of the claims.

With respect to adequate disclosure Applicants are referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175) regarding disclosure. For adequate disclosure, like enablement, requires *representative examples*, which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that

applicant had possession of the full scope of the claimed invention. See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and University *of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure.

Here, the general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe that vast majority of methods and variegated genomes that could be used to produce the claimed libraries, listing examples a few examples of "tri-molecular" recombination employing "vaccinia virus" is not sufficient to teach the broader genus.

In addition, Applicants specification does not provide any general teaching that would allow a person of skill in the art to extend the "tri-molecular" recombination concept using "vaccinia virus" to other areas. For example, the prior art teaches that libraries of polynucleotides that encode potential antigen-specific human immunoglobulins generally cannot be produced using "traditional" methods of homologous recombination with poxviruses like vaccinia (e.g., see specification, page 8, paragraph 20, "Although traditional homologous recombination in poxviruses [e.g., vaccinia] is useful for expression of previously isolated foreign DNA in a poxvirus, the method ***is not conducive to the construction of libraries***, since the overwhelming majority of viruses recovered have not acquired a foreign DNA insert. Using traditional homologous recombination, the recombination efficiency is in the range of approximately

0.1% or less") (emphasis added). In addition, other attempts to increase the efficiency proved to be unsuccessful and/or unpredictable (e.g., see specification, page 9, paragraph 22, wherein "direct ligation" was shown to be unsatisfactory, "Although large DNA fragments are efficiently cloned into the genome [via direct ligation], proteins encoded by the DNA insert will only be expressed at the low level ... In addition, the DNA will be inserted in both orientations at the NotI site, and therefore might not be expressed at all").

Furthermore, a person of skill in the art would not expect all vectors to behave the same (e.g., plant viruses require different considerations than animal viruses and double stranded DNA does not behave the same as single stranded RNA). For example, "A major problem that has hampered the use of retroviruses as library vectors has been the tendency of viruses with different inserts to exhibit substantially different titers. Thus, preservation of equal representation in the library, a difficult task even when comparatively simple plasmid-based systems are used, becomes an especially important consideration. At least two potential ways exist in which insert DNA can influence titer in a recombinant retrovirus. The first is based on the unavoidable linkage between RNA expression and titer. If the insert, either as DNA or RNA, confers instability on the viral RNA, or otherwise acts to impede its creation or packaging, the reduced expression directly translates into reduced representation. This is not the case for a plasmid-based libraries, for example, in which reduced expression can make detection of a desired product difficult, but does not, in itself, affect representation. The second is based on the linkage between the efficiency of reverse transcription and titer. If the insert, as RNA, resists reverse transcription (e.g., because it contain extended regions of self-

complementarity) this will also result in under-representation. Most RNAs have not been selected for compatibility with the viral life cycle, and so it is not surprising to find wide variation in the efficiency of their reverse transcription in vivo" (see Seed, B. "Developments in expression cloning" Current Opinion in Biotechnology 1995, 6: 567-573, especially page 570, column 1, third paragraph).

Thus, the prior art teaches that only poxvirus vectors that possess genomes capable of undergoing "tri-molecular" recombination [i.e., the "two" v7.5/tk vaccinia virus genome fragments produced using the NotI/ApaI restriction enzymes] will reliably produce recombinants at an efficiency that is amenable for polynucleotide library construction (e.g., see specification, page 9, paragraph 23, "***poxvirus vectors were previously not used*** to identify previously unknown genes of interest from a complex population of clones, because a high efficiency, high titer-producing method of cloning did not exist for pox viruses ... [***until***] the present inventor developed a method for generating recombinant poxviruses using ***tri-molecular recombination*** [i.e., only vaccinia virus vectors that are amendable to "tri-molecular" recombination will work]"). Consequently, one of skill in the art would reasonably conclude that Applicants were in possession of methods for selecting polynucleotide which encode an intracellular immunoglobulin molecule, or fragment thereof, using only materials and method steps that are required for "tri-molecular" recombination with "vaccinia virus" vectors. Thus, applicants were not in possession of the "full scope" of the claimed invention.

18. Claims 1-20, 22, 24-27, 29-35, 38, 40-41, 44 and 59-62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of selecting polynucleotides which encode an intracellular immunoglobulin molecule via homologous recombination using "two" non-overlapping fragments of the cleaved v7.5/tk or vEL/tk virus genomes produced using NotI/ApaI restriction enzymes and "one" transfer plasmid containing TKL/TKR and a library of human immunoglobulin genes containing both heavy and light genes (i.e. "tri-molecular" recombination process, see specification, page 10, paragraph 27; see also page 151, paragraph 363) using "vaccinia virus" vectors, is not enabled for a method employing any vector genome produced via any method. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". Some of these factors may include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) The breadth of the claims and the nature of the invention: The claims are drawn to a broad genus. The scope of these claims includes an enormous number of methods for producing and/or selecting intracellular immunoglobulins using an enormous number of potential vectors (e.g., see specification, page 54, paragraph 223, "In constructing antibody libraries in eukaryotic cells, any standard vector which allows expression in eukaryotic cells may be used"; see also paragraph 124 reciting a large "laundry list" of potential examples e.g., plant, animal, RNA, DNA, etc.). Consequently, the nature of the invention cannot be fully determined.

(3 and 5) The state of the prior art and the level of predictability in the art: The prior art teaches that libraries of polynucleotides that encode potential intracellular immunoglobulins generally cannot be produced using "traditional" methods of homologous recombination with poxviruses like vaccinia (e.g., see specification, page 8, paragraph 20, "Although traditional homologous recombination in poxviruses [e.g., vaccinia] is useful for expression of previously isolated foreign DNA in a poxvirus, the method ***is not conducive to the construction of libraries***, since the overwhelming majority of viruses recovered have not acquired a foreign DNA insert. Using traditional homologous recombination, the recombination efficiency is in the range of approximately 0.1% or less") (emphasis added). In addition, other attempts to increase the efficiency proved to be unsuccessful and/or unpredictable (e.g., see specification, page 9, paragraph 22, wherein "direct ligation" was shown to be unsatisfactory, "Although large DNA fragments are efficiently cloned into the genome [via direct ligation], proteins encoded by the DNA insert will only be expressed at the low level ... In addition, the DNA will be

inserted in both orientations at the NotI site, and therefore might not be expressed at all"). Thus, the prior art teaches that only poxvirus vectors that possess genomes capable of undergoing "tri-molecular" recombination [i.e., the "two" v7.5/tk vaccinia virus genome fragments produced using the NotI/ApaI restriction enzymes] will reliably produce recombinants at an efficiency that is amenable for polynucleotide library construction (e.g., see specification, page 9, paragraph 23, "***poxvirus vectors were previously not used*** to identify previously unknown genes of interest from a complex population of clones, because a high efficiency, high titer-producing method of cloning did not exist for pox viruses ... [***until***] the present inventor developed a method for generating recombinant poxviruses using ***tri-molecular recombination*** [i.e., only vaccinia virus vectors that are amendable to "tri-molecular" recombination will work]").

Furthermore, a person of skill in the art would not expect all vectors to behave the same (e.g., plant viruses require different considerations than animal viruses and double stranded DNA does not behave the same as single stranded RNA). For example, "A major problem that has hampered the use of retroviruses as library vectors has been the tendency of viruses with different inserts to exhibit substantially different titers. Thus, preservation of equal representation in the library, a difficult task even when comparatively simple plasmid-based systems are used, becomes an especially important consideration. At least two potential ways exist in which insert DNA can influence titer in a recombinant retrovirus. The first is based on the unavoidable linkage between RNA expression and titer. If the insert, either as DNA or RNA, confers instability on the viral RNA, or otherwise acts to impede its creation or packaging, the reduced expression

directly translates into reduced representation. This is not the case for a plasmid-based libraries, for example, in which reduced expression can make detection of a desired product difficult, but does not, in itself, affect representation. The second is based on the linkage between the efficiency of reverse transcription and titer. If the insert, as RNA, resists reverse transcription (e.g., because it contain extended regions of self-complementarity) this will also result in under-representation. Most RNAs have not been selected for compatibility with the viral life cycle, and so it is not surprising to find wide variation in the efficiency of their reverse transcription in vivo" (see Seed, B. "Developments in expression cloning" Current Opinion in Biotechnology 1995, 6: 567-573, especially page 570, column 1, third paragraph).

(6-7) The amount of direction provided by the inventor and the existence of working examples: Applicants disclose the use of examples that contain "two" non-overlapping fragments of the v7.5/tk virus genome produced using the NotI and ApaI restriction enzymes and "one" recombinant plasmid containing TKL/TKR and the library of human immunoglobulin genes to produce the "vaccinia virus" vectors.

(8) The quantity of experimentation needed to make or use the invention base on the content of the disclosure: As a result of the broad and unpredictable nature of the invention and the lack of specific guidance from the specification, the Examiner contends that the quantity of experimentation needed to make and or use the invention would be great. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445

* n.23 (Fed. Cir. 19991). In this case, Applicants have not provided any working examples that would teach this enormous genus that falls within a highly unpredictable art area. Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

Claims Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

19. Claims 27, 29, 30, 31, 32, 33, 34, 35, 38, 40, 41 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. **Claim 27** recites the limitation "the naturally-occurring genome" in the first line. There is insufficient antecedent basis for this limitation in the claim. Therefore, claim 27 and all dependent claims are rejected under 35 USC 112, second paragraph.

B. **Claim 35** recites the limitation "said host cells" in the first line. There is insufficient antecedent basis for this limitation in the claim because more than one host cell is referred to in the independent claim (e.g., see claim 1 wherein a variety of host cells are disclosed; see also claim 18 wherein "eukaryotic" host cells are disclosed).

Therefore, claim 35 and all dependent claims are rejected under 35 USC 112, second paragraph.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

22. Claims 1-20, 22, 24-27, 29-35, 38, 40-41, 44 and 59-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rowlands et al. (WO 93/01296) (Date of Patent is **January 21, 1993**) and Zauderer et al. (WO 00/28016) (Date of Patent is **May 18, 2000**) and Waterhouse et al. (Waterhouse, P.; Griffiths, A.D.; Johnson, K.S.; Winger, G. "Combinatorial infection and in vivo recombination: a strategy for making large phage antibody repertoires" *Nucleic Acids Research*, **1993**, 21, 9, 2265-2266) as evidenced by Roitt et al. (Roitt, I.; Brostoff, J.; Male, D.

Immunology Sixth Edition. New York: Mosby 2001, page 67) and as also evidenced by Applicants' specification.

For ***claims 1 and 4***, Rowlands et al. (see entire document) teach a method for producing antibodies in vaccinia infected cells including intracellular antibodies that reads on the presently claimed invention (e.g., see Rowlands et al., abstract; see also paragraph bridging pages 15-16 showing production of "intracellular" antibodies i.e., both heavy and light chains found within the cell and thus said host cells are "capable" of expressing intracellular immunoglobulin molecules; see also page 6, paragraph 3). For example, Rowlands et al. teach **[a-d]** the use of a population of mammalian host cells i.e., "eukaryotic" host cells (e.g., see page 4, paragraph 2; see also page 8, paragraph 1) for introducing and expressing a first/second polynucleotide encoding, through operable association with a transcriptional control region a first/second immunoglobulin polypeptide comprising both heavy/light chain constant/variable regions and a signal peptide for secretion using a vaccinia virus vector (e.g., see claim 9, "A process ... compris[ing] ... transfecting the infected cells with a transfer vector [i.e., introducing a polynucleotide] containing DNA encoding the light and ... heavy chain of the antibody under control of a suitable promoter"; see also page 2, middle paragraph, "An antibody molecule is composed of two light chains and two heavy chains ... Each heavy chain has at one end a variable domain followed by a number of constant domains, and each light chain has a variable domain at one end and a constant domain at the other end"; see especially page 4, second full paragraph, "It has now been found that vaccinia virus vectors can be used for expression of the light and heavy chains of a recombinant

antibody in a suitable host cell and that a proportion of the chains combine within the cell to form a recombinant antibody which is secreted into the medium and can thus be recovered in functional form"). Rowlands et al. further disclose **[d]** permitting expression of said plurality of intracellular immunoglobulin molecules, or fragments thereof, under conditions wherein said modified phenotype can be detected (e.g., see page 5, last paragraph wherein the use of "selectable markers" is disclosed, "The transfer vector contains DNA encoding the light chain and/or the heavy chain of an antibody together with a suitable promoter and the selectable marker will also be under control of a suitable promoter"; see also page 5, second to last paragraph, "Suitable selectable markers ... include ... guanine phosphoribosyltransferase (gpt) gene which allows ... growth of the infected cells [and thus permits the expression of said immunoglobulin molecules] in the presence of mycophenolic acid [i.e., a modified phenotype, which is detected by cell growth]"). Finally, Rowlands et al. disclose **[e]** recovering the vaccinia virus vectors containing polynucleotides of said first library from those individual host cells which exhibit said modified phenotype (e.g., see page 5, paragraph 1, step 4, wherein the virus is "harvested" several times [i.e., recovered and/or isolated]).

For ***claim 9***, Rowlands et al. disclose human and "humanized" antibodies (e.g., see claims 2 and 4; see also page 8, last paragraph, "However, the invention is most preferably applied to the production of human antibodies").

For ***claims 10-17***, Rowlands et al. disclose both heavy and light constant/variable region (e.g., see page 2, middle paragraph, "An antibody molecule is composed of two light chains and two heavy chains ... Each heavy chain has at one end a variable domain

followed by a number of constant domains"; see also pages 11-12, Example 1, especially page 12, paragraph 1; see also page 16, Example 5). Rowlands et al. do not explicitly state that lambda or kappa light chains are employed, but the examiner contends that this would be immediately envisioned in accordance with *In re Schauman*.

In *In re Schauman*, 572 F.2d 312, 197 USPQ 5 (CCPA 1978), claims to a specific compound were anticipated because the prior art taught a generic formula embracing a limited number of compounds closely related to each other in structure and function. Here, Rowlands et al. disclose a generic claim drawn to a light chain antibody that contains only two possible structurally related species (i.e., kappa and lambda chains) and, as a result, a person of skill in the art would immediately envision these possibilities.

In the alternative, the Examiner contends that Rowlands et al. inherently disclose the lambda and kappa chains because the light chains of most vertebrates have been shown to exist in only two distinct forms (e.g., see Roitt et al., page 67, column 2, second full paragraph). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The Office does not have the facilities to make such a comparison and the burden is on the applicants to establish the difference. See *In re Best,* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

For ***claims 18-20 and 24-27, 29-35, 38***, Rowlands et al. disclose the "eukaryotic" vaccinia poxvirus vector (e.g., see page 13, Example 3). Rowlands et al. do not explicitly state that the vaccinia virus is a linear, double-stranded DNA othopoxvirus vector.

However, the Examiner contends that these would be inherent features of the virus as disclosed by Applicants' specification (e.g., specification, page 6, paragraph 13 demonstrating that vaccinia poxvirus is a "eukaryotic" vector; see also pages 6-7; see especially page 63, paragraph 144, "The naturally-occurring vaccinia virus genome is a cross-linked, double stranded linear DNA molecule"; see also page 62, paragraph 142, disclosing vaccinia to be an orthopoxvirus). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The Office does not have the facilities to make such a comparison and the burden is on the applicants to establish the difference. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

For ***claim 40, 41 and 44***, Rowlands et al. disclose a T7 phage promoter active in cells in which T7 RNA polymerase is expressed (e.g., see page 8, paragraph 2, "Expression levels of the two chains of the antibody can be enhanced by use of T7 polymerase to amplify the gene under the control of the T7 promoter"; see also claim 6 wherein p7.5k, 11k and 19k are disclosed).

The prior art teachings of Rowlands et al. differ from the claimed invention as follows:

For ***claim 1***, Rowlands et al. are deficient in that they do not specifically teach the use of a "library" of first/second polynucleotides.

For ***claims 2-8 and 10-20***, Rowlands et al. do not disclose repetitive steps (f)-(j), (k)-(o) and (p)-(t) for "biopanning" a library including isolating/recovering said polynucleotides for use in subsequent rounds of biopanning for library "enrichment" of the "focused" libraries associated with the subsequent screening steps.

For ***claim 22***, Rowlands et al. do not disclose an MOI of 1.

For claims ***59-61***, Rowlands et al. do not disclose heterologous polynucleotides within the library wherein said heterologous polynucleotide is common to each member of the library or its fusion to the first intracellular immunoglobulin subunit polypeptides such as a targeting sequence

However, Zauderer et al. and Waterhouse et al. teach the following limitations that are deficient in Rowlands et al.:

For ***claim 1***, Zauderer et al. (see entire documents) teach the use of a "library" of polynucleotides in a vaccinia virus vector using the "tri-molecular recombination" approach for screening purposes (e.g., see Zauderer et al., page 52, lines 13-16, "The high yield of viral recombinants in tri-molecular recombination makes it possible, for the first time, to efficiently construct genomic or cDNA libraries in a vaccinia virus derived vector"; see also page 15, paragraph 1; see also page 22, last two paragraphs; see also Example 6 on pages 42-52). In addition, Waterhouse et al. teach that a "library" can be usefully employed to screen for antibodies with high affinity to various antigens including the use of heavy/light chains that are "packaged together" (see Waterhouse et al., page 2265, column 1; see also paragraph bridging pages 2265-2266). Furthermore, Zauderer et al. also disclose modified phenotypes including Applicants' elected "cell

death" species (e.g., see Zauderer et al., page 34, line 14, "Alternatively, recombinant viruses with 'suicide' characteristics may be constructed").

For ***claims 2-8, 10-20***, Zauderer et al. disclose steps for introducing said vectors into host cells, permitting the expression of said vectors, contacting said expressed antibodies with an antigen and recovering said vectors can be repeated as needed to increase the specificity and/or binding affinity i.e., they use "biopanning" techniques (e.g., see page 23, last paragraph through page 24, first paragraph, especially lines 8-10, "The above-described protocol is repeated or more cycles, to increase the level of enrichment obtained by this procedure"). Zauderer et al. disclose "isolating" the polynucleotides contained in the vaccinia virus vectors (e.g., see Zauderer et al., page 52, lines 20-23; see also page 23, last paragraph through page 24, first paragraph, especially lines 8-10, "The above-described protocol is repeated or more cycles, to increase the level of enrichment obtained by this procedure [i.e., involves combining isolated fractions]").

For ***claim 22***, Zauderer et al. disclose, for example, an MOI = 1 (e.g., see page 86, line 2).

For ***claims 59-61***, Zauderer et al. disclose, for example, the use of histidine tags which represent common heterologous fusion targeting sequences (e.g., see page 33, line 13).

It would have been obvious to one skilled in the art at the time the invention was made to make a library of vaccinia virus vectors as taught by Zauderer et al. to express fully functional antibodies as taught by Rowlands et al. for the purpose of screening

and/or affinity maturation as taught by Waterhouse et al. because Zauderer et al. explicitly state that their libraries can be efficiently produced using the tri-molecular recombination approach with the vaccinia virus vectors (like the vaccinia virus vectors disclosed by Rowlands et al.) and Waterhouse et al. teach that such a library would be useful in screening and affinity maturation. Thus, one of ordinary skill in the art would have been motivated to make the libraries as taught by Zauderer et al. using the heavy/light chain antibodies as disclosed by Rowlands et al. because Zauderer et al. explicitly state that the their "tri-molecular" approach represents an easy and efficient means for generating a library in vaccinia virus vectors in mammalian cells, which is a preferred embodiment for Rowlands et al. (e.g., see Zauderer et al., page 22, lines 14-17, "Major advantages of these infectious [vaccinia] viral vectors are ... the ease and efficiency with which recombinants can be introduced mammalian cells"). In addition, Waterhouse et al. teach that "associated" light and heavy chains are a "preferred" embodiment for screening and/or affinity maturation because they can be "simultaneously co-selected" (e.g., see Waterhouse et al., page 2265, paragraph 2), which would encompass the "associated" heavy/light chains described by Rowlands et al. Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because Zauderer et al. teach several successful examples of library formation using the same vaccinia virus vectors that are disclosed by Rowlands et al. and Waterhouse et al. teach several successful examples of associated light/heavy chains that can be used for screening and/or antibody maturation, which would encompass the heavy/light chain antibodies disclosed by Rowlands et al.

23. Claims 1-20, 22, 24-27, 29-35, 38, 40-41, 44 and 59-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rowlands et al. (WO 93/01296) (Date of Patent is **January 21, 1993**) and Zauderer et al. (WO 00/28016) (Date of Patent is **May 18, 2000**) and Waterhouse et al. (Waterhouse, P.; Griffiths, A.D.; Johnson, K.S.; Winger, G. "Combinatorial infection and in vivo recombination: a strategy for making large phage antibody repertoires" *Nucleic Acids Research*, **1993**, 21, 9, 2265-2266) and Marasco (Marasco, W. A. "Intrabodies: turning the humoral immune system outside in for intracellular immunization" *Gene Therapy* **1994**, *4*, 11-15) as evidenced by Roitt et al. (Roitt, I.; Brostoff, J.; Male, D. Immunology Sixth Edition. New York: Mosby 2001, page 67) and as also evidenced by Applicants' specification.

For ***claims 1-20, 22, 24-27, 29-35, 38, 40-41, 44 and 59-61***, Rowlands et al. and Zauderer et al. teach all the limitations stated in the 35 U.S.C. 103(a) rejection above (incorporated in its entirety herein by reference), which renders obvious claims 1-20, 22, 24-27, 29-35, 38, 40-41, 44 and 59-61.

The prior art teaching of Rowlands et al. and Zauderer et al. differs from the claimed invention as follows:

For ***claim 62***, the combined prior art teachings of Rowlands et al. and Zauderer et al. differ from the claimed invention by not reciting the use of targeting sequences capable of localizing said intracellular immunglobulin molecule.

However, Marasco teaches the following limitations that are deficient in the combined teachings of Rowlands et al. and Zauderer et al.:

For ***claim 62***, Marasco (see entire document) teaches, for example, localization in the endoplasmic reticulum using a KDEL-tagged sFv intrabody (e.g., see Marasco, page 12,).

It would have been obvious to one skilled in the art at the time the invention was filed to screen the libraries of antibodies disclosed by the combined teachings of Rowlands et al. and Zauderer et al. using intracellularly expressed and/or localized antibodies like the KDEL-tagged sFV disclosed by Marasco because Marasco explicitly states that such "intrabodies" represent a "... powerful new family of protein molecules that have potential application in the gene therapy of a number of human diseases" (e.g., see Marasco, page 11, column 2, paragraph 1; see also abstract wherein cancer and infectious diseases are disclosed). Furthermore, one of ordinary skill in the art would have been motivated to use intracellular expression of antibodies because, for example, they would allow for the down-regulation of growth factor receptors like interleukin-2 (e.g., see page 12, column 1), provide for a defense against tumors (e.g., see page 12, column 2), modulate enzyme function (e.g., see page 12, column 1), treat cancer and or other infectious diseases (e.g., see abstract), inactivate cytosolic oncoproteins (e.g., see page 13, column 1), inhibit virus replication (e.g., see page 13, column 2), etc. Finally, one of ordinary skill in the art would have reasonably expected to be successful because Marasco teaches that "the creation of large human immunoglobulin libraries [like the in vitro libraries disclosed by the combined teachings of Rowlands et al. and Zauderer et al.] ... has allowed investigators to bypass in vivo immunization and produce high-affinity human antibodies to human proteins" (see Marasco, page 11, Introduction; see also

abstract, "Recent advances in antibody engineering have now allowed the genes encoding antibodies to be manipulated so that the antigen binding domain can be expressed intracellularly").

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

24. Claims 1-20, 22, 24-27, 29-35, 38, 40-41, 44 and 59-62 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 84-122 and 127-131 of U.S. Patent Application Serial No. 09/984,456 (referred to herein as '456) and Marasco (Marasco, W. A. "Intrabodies: turning the humoral immune system outside in for intracellular immunization" *Gene Therapy* **1994**, *4*, 11-15).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examiner application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d

1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1986).

Here, claims 84-122 and 127-131 '456 recite a method for selecting polynucleotides which encode immunoglobulin molecules which is essentially the same as that disclosed by claims 1-20, 22, 24-27, 29-35, 38, 40-41, 44 and 59-62 in the present application (e.g., both methods disclose eukaryotic host cells, a first and second library of polynucleotides encoding immunglobulin light/heavy chain constant/variable regions, permitting expression of said immunoglobulin molecules, contacting the molecules with an antigen, recovering the polynucleotides that encode for immunoglobulins that bind to said antigens, etc). The method of claims '456 differ from the present application in that they claim "extracellular" as opposed to "intracellular" expression as currently claimed (e.g., "signal" sequences are claimed in '456).

However, Marasco teaches the use of "intracellular" expression and localization of antibodies for screening and pharmaceutical applications (e.g., see Marasco, abstract and Introduction).

Thus, it would have been obvious to modify the method of claims 84-122 and 127-131 of '456 such that "intracellular" expression and/or localization occurs because Marasco teaches that "extracellular" expression may be obtained within Applicants' preferred "phage" vectors (e.g., see claim 18 wherein a eukaryotic virus vector is disclosed; see also specification, page 54, paragraph 123 where Applicants define "vectors" to any standard vector which allows expression in eukaryotic cells may be used [including] ... phage"; compare to Marasco, Introduction, "Using these tools, the creation

of large human immunoglobulin libraries from naive individuals has been achieved and when combined with phage display technology, has allowed investigators to bypass in vivo immunization and produce high-affinity human antibodies to human proteins") (emphasis added). Furthermore, one of ordinary skill in the art would have been motivated to use intracellular expression and/or localization of antibodies because, for example, they would allow for the down-regulation of growth factor receptors like interleukin-2 (e.g., see page 12, column 1), provide for a defense against tumors (e.g., see page 12, column 2), modulate enzyme function (e.g., see page 12, column 1), treat cancer and or other infectious diseases (e.g., see abstract), inactivate cytosolic oncoproteins (e.g., see page 13, column 1), inhibit virus replication (e.g., see page 13, column 2), etc. Finally, one of ordinary skill in the art would have reasonably expected to be successful because Marasco teaches that "the creation of large human immunoglobulin libraries [like the in vitro libraries disclosed by the combined teachings of Rowlands et al. and Zauderer et al.] ... has allowed investigators to bypass in vivo immunization and produce high-affinity human antibodies to human proteins" (see Marasco, page 11, Introduction; see also abstract, "Recent advances in antibody engineering have now allowed the genes encoding antibodies to be manipulated so that the antigen binding domain can be expressed intracellularly").

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

25. Claims 1-20, 22, 24-27, 29-35, 38, 40-41, 44 and 59-62 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 46-133 of U.S. Patent Application Serial No. 10/465,808 (referred to herein as '808) and Marasco (Marasco, W. A. "Intrabodies: turning the humoral immune system outside in for intracellular immunization" *Gene Therapy* **1994**, *4*, 11-15).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examiner application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1986).

Here, claims 46-133 of '808 recite a method for selecting polynucleotides which encode immunoglobulin molecules which is essentially the same as that disclosed by claims 1-20, 22, 24-27, 29-35, 38, 40-41, 44 and 59-62 in the present application (e.g., both methods disclose eukaryotic host cells, a first and second library of polynucleotides encoding immunglobulin light/heavy chain constant/variable regions, permitting expression of said immunoglobulin molecules, contacting the molecules with an antigen, recovering the polynucleotides that encode for immunoglobulins that bind to said antigens, etc). The method of claims '808 differ from the present application in that they claim "extracellular" as opposed to "intracellular" expression as currently claimed (e.g., "signal" sequences are claimed in '808).

However, Marasco teaches the use of "intracellular" expression and localization of antibodies for screening and pharmaceutical applications (e.g., see Marasco, abstract and Introduction).

Thus, it would have been obvious to modify the method of claims 46-133 of '808 such that "intracellular" expression and/or localization occurs because Marasco teaches that "extracellular" expression may be obtained within Applicants' claimed "phage" vectors (e.g., see claim 18 wherein a eukaryotic virus vector is disclosed; see also specification, page 54, paragraph 123 where Applicants define "vectors" to any standard vector which allows expression in eukaryotic cells may be used [including] ... phage"; compare to Marasco, Introduction, "Using these tools, the creation of large human immunoglobulin libraries from naive individuals has been achieved and when combined with phage display technology, has allowed investigators to bypass in vivo immunization and produce high-affinity human antibodies to human proteins") (emphasis added). Furthermore, one of ordinary skill in the art would have been motivated to use intracellular expression and/or localization of antibodies because, for example, they would allow for the down-regulation of growth factor receptors like interleukin-2 (e.g., see page 12, column 1), provide for a defense against tumors (e.g., see page 12, column 2), modulate enzyme function (e.g., see page 12, column 1), treat cancer and or other infectious diseases (e.g., see abstract), inactivate cytosolic oncoproteins (e.g., see page 13, column 1), inhibit virus replication (e.g., see page 13, column 2), etc. Finally, one of ordinary skill in the art would have reasonably expected to be successful because Marasco teaches that "the creation of large human immunoglobulin libraries [like the in

vitro libraries disclosed by the combined teachings of Rowlands et al. and Zauderer et al.] ... has allowed investigators to bypass in vivo immunization and produce high-affinity human antibodies to human proteins" (see Marasco, page 11, Introduction; see also abstract, "Recent advances in antibody engineering have now allowed the genes encoding antibodies to be manipulated so that the antigen binding domain can be expressed intracellularly").

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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